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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,432	06/04/2001	Seth P. Finklestein	00786-400002	4601

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,432	FINKLESTEIN, SETH P.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,17,18 and 25-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,17,18 and 25-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 01, 2003 has been entered.

Response to Amendment

2. Claim 38 has been amended as requested in the amendment of Paper filed on December 01, 2003. Claims 1-6, 17, 18 and 25-43 are pending in the instant application.

Claims 1-6, 17, 18 and 25-43 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on December 01, 2003 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Information Disclosure Statement

6. The information disclosure statement filed on December 01, 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication

or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. In the instant case it appears that no copies of the listed documents have been provided. The IDS has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 103

7. Claims 1-6, 17-18 and 25-43 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Reynolds et al. (WO 98/221127, May, 1998) in view of Peng et al. (April, 1998, J. Cerebral Blood Flow and Metabolism, 18, pp.349-360) for reasons of record as applied to claims 1-6 and 14-18 in section 3 of Paper No. 8 and also reasons of record in section 6 of Paper No. 11.

Applicant reviews MPEP sections relevant to rejection based on obviousness and submits that "neither Reynolds nor Peng suggest that their treatment regimes should be modified (to the contrary!), and there is no reasonable expectation for success" (pages 7 and 8 of the Response). Applicant argues that the instant "claims are limited to a particular treatment regime, one in which an EGF-like polypeptide is administered commencing (*i.e.*, beginning) more than 6, 12, or 24 hours after an injury to the central nervous system" (last paragraph at page 7). These arguments have been fully considered but were not found to be persuasive for the following reasons.

According to the publication of Peng et al. "Cerebroventricular infusion of EGF (24 or 120 ng/d) for 7 days to gerbils starting 2 hours before or immediately after transient forebrain ischemia caused a significant prolongation of response latency time in a passive avoidance task

in comparison with the response latency of vehicle treated ischemic animals" (abstract of the document, emphasis added by the Examiner). Thus, in Peng et al. protocol administration of EGF started immediately after the injury to the central nervous system and continued for 7 days after the injury. The administration of EGF, as concluded in Peng et al. publication, led to reduction of a neurological deficit, which resulted from the injury to the central commencing at 6, 12 or 24 hours after the injury, the instant rejection would have been made under appropriate section of 35 U.S.C. 102.

The Examiner maintains the position that a *prima facie* case of obviousness is fully established in the instant case. First, publication of Peng et al. clearly establishes the beneficial neuroprotective effect of EGF ("EGF has a neuroprotective effect on ischemic hippocampal neurons *in vivo* possibly through inhibition of free radical neurotoxicity and lipid peroxidation" see the abstract, for example). Second, there are no teachings in the prior art that would suggest that the established neuroprotective action of EFG is only effective when administered before or immediately after the trauma. Therefore, one skilled in the art would have no reasons to expect that the central nervous system would be refractive to the action of EGF if administration started not immediately but after a certain interval after an injury occurred and, for that reason, there is a reasonable expectation of success in modifying the regime of Peng et al. and begining administration of EGF at different time points after an injury to CNS.

Next, because a neuroprotective effect of EGF has been established, one of ordinary skill in the art would readily appreciate the obvious advantage to use EGF to treat an injury to the central nervous system any time after the injury, including "more than 6, 12, or 24 hours after an injury to the central nervous system" (bottom at page 7 of the Response). Moreover, in a real life

situation a skilled practitioner would be motivated to administer EGF to a patient with a trauma to the nervous system as soon as possible within up to 7 days after the injury in order to achieve a beneficial action of EGF.

Applicant submits that according to an article in Boston Globe published "in February 1999, the longest known treatment [of a stroke] window was reported to be three hours; extension of that window to six hours (as Applicant has previously claimed) was considered a new and ground breaking (or, at least, news worthy) event" (bottom at page 9 of the Response). Applicant further argues that "the fact that Reynolds or Peng may have continued their treatment to, and even beyond, Applicant's starting point, is of no consequence" (middle at page 10). These arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant is advised that Boston Globe publication is not a peer-reviewed article; therefore, one skilled in the art would not consider determination of treatment protocol based on a newspaper article. The article, however, appears to address"3-hour stroke therapy window" with regard to formation of blood clots and their consequences to strokes, which is not the mechanism discussed in Peng publication. Based on the information presented in Peng article, a skilled artisan would be motivated to use EGF because it "has a neuroprotective effect on ischemic hippocampal neurons *in vivo* possibly through inhibition of free radical neurotoxicity and lipid peroxidation", the effect that appears to be beneficial for a long-term treatment of patients who have suffered an injury to CNS. The Examiner maintains that publication of Peng et al. is of a particular consequence because it reported a beneficial effect of EGF administration during seven days after an ischemic event. One skilled in the art would have been motivated to

use EGF polypeptide based on publications of Peng and Reynolds to treat a patient who has suffered an injury to the central nervous system as soon as possible within at least 7 days after the injury occurred in order to achieve a neuroprotective effect of EGF, and this time interval includes 6 , 12 and 24 hours recited in the claims of the instant specification..

Conclusion

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.